

**REMARKS/ARGUMENTS**

Claims 1, 2, 6, 7, 27 and 28 are pending and examined. Claims 29-34 are newly added. The phrase "at least one position selected from the group consisting of -1, 1, 2, 3, 5 and 6 and at least one position selected from the group consisting of -1, 1, 2 and 3 in first and second adjacent fingers" has been deleted from claim 1 as redundant in view of the later recitation in the same claim requiring at least partial randomization at positions 6 and 2 respectively. If position 6 is at least partially randomized, it necessarily follows that at least one position selected from the group consisting of -1, 1, 2, 3, 5, and 6 has been at least partially randomized; likewise if position 2 is at least partially randomized it necessarily follows that at least one position selected from the groups consisting of -1, 1, 2 and 3 has been at least partially randomized. Claim 1 (as amended) and new claims 29 and 30 define groups of amino acids to which partial randomization is restricted. These groups are those described as being preferred in Table 1 at p. 11 of the specification. New claims 30-34 parallel existing claims 1, 2, 6, 27 and 28 respectively except that claim 31 defines the amino acids occupying position 6 rather than position 2 as in claim 1. Applicants now turn to the Examiner's comments.

**1. The Information Disclosure Statement**

The Examiner's comment to the effect that an Interview Summary Record was attached to a restarted office action of December 2, 2003 are acknowledged. However, no office action dated December 2, 2003 is of record in the case. An office action dated December 20, 2002 is of record, but review of applicants' file indicates no Interview Summary Record was attached to this either. In any event, the information disclosure statement has now been considered.

**2. Priority**

Applicants disagree with the Examiner's remarks concerning priority. However, the issue of priority is not relevant to the issues now pending.

### 3. Claim rejections under 35 USC 103

Claims 1, 2, 6-7 and 27-28 stand rejected as allegedly obvious over Greisman in view of Choo. Applicants maintain the distinctions over the cited references described in their appeal brief, and will resubmit them on appeal if necessary. However, it is submitted that such should be unnecessary in view of the amendment of the claim specifying sets of amino acids to which partial randomization is restricted.

As previously noted the present application provides the insight that varying positions 6 and 2 together is advantageous in generating additional specificities not obtained by varying a single finger alone because these residues contact the same base pair of a target (specification at p. 9, lines 5-9). However, only certain residues occupying positions 6 and 2 are able to act in combination to result in zinc finger proteins with sequence specific binding. Restriction of partial randomization to such amino acids is advantageous, both because it increases the representation of productive combinations of amino acids at these positions, and because it allows greater variation at other positions without exceeding constraints on overall library size.

In addition to the reasons already of record for nonobviousness, the cited references do not teach or suggest the groups of amino acids recited in claim 1 to which partial randomization of amino acids is restricted. Greisman teaches to randomize in such a manner as to allow any of sixteen amino acids at each position (footnote 15 of Greisman). The four omitted amino acids are omitted as part of a strategy to avoid stop codons (*id.*). Choo does not explicitly disclose whether he restricted randomization to certain codons. However, reference to his earlier work cited in the Choo paper (see reference 7<sup>1</sup> of the Choo paper cited at p. 4321 first column, fourth paragraph of the Choo paper) shows that he, like Greisman, restricted randomization to sixteen amino acids. A patent by Choo, US 6,007,988 (of record) also omitted four amino acids and explained that the reason was to avoid stop codons ("T in the first base position is omitted in order to avoid stop codons, but this has the *unfortunate* effect that the codons for Trp, Phe, Tyr and Cys are not represented" (at col. 12, 24-27, emphasis supplied)).

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<sup>1</sup> Choo, PNAS 91, 11163-11167 (1994) (#78 on IDS) at p. 11164, second column third paragraph.

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The view that omitting the above amino acids was "unfortunate" teaches away from performing randomization with additional amino acids omitted. None of the references teaches the claimed groups of amino acids to which randomization should be restricted.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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